Central Nervous System Vasculitis in a Patient with Myelodysplastic Syndrome

Mobini Maryam, Khosravi Sahar, Khajavi Mohammad
Internal Medicine Department, Imam Khomeini Hospital, Mazandaran University of Medical Sciences, Sari, Iran

Corresponding author: Maryam Mobini, MD
Rheumatologist, Assistant Professor of Internal Medicine Department, Imam Khomeini Hospital, Razi St., Mazandaran University of Medical Sciences, Sari, Iran; 48166-33131
Tel: 0151- 2261700-4
Fax: 0151- 2264044
Mobile: 09111521030
E-mail: mmobini50@yahoo.com

Abstract:
Myelodysplastic syndromes (MDS) are a group of hematological disorders ranging from chronic refractory anemia to leukemia. There are some reports about association of MDS with autoimmune disorders and vasculitis. In this study we describe a patient with MDS and vasculitis presenting with central nervous system (CNS) involvement. A clinical response to immunosuppressive therapy was also observed in the patient.

Key words: Anemia, Vasculitis, Cerebrovascular Accident

Introduction

Myelodysplastic syndromes (MDS) include a heterogeneous group of hematological disorders with quantitative changes of one or more blood and bone marrow elements.

There are some reports about association of MDS with autoimmune disorders such as polymyalgia rheumatica, relapsing polychondritis,(1) rheumatoid arthritis,(2) Sjogren syndrome,(1, 2) nephritic syndrome,(3) polymyositis,(4) Behcet disease(5) and some types of vasculitis such as cutaneous vasculitis,(1, 2, 4, 6-8) polyarthritis nodosa,(7, 8) Wegner granulomatosis, microscopic polyangitis, Henoch Schonlein purpura(8) and large vessel vasculitis.(9)

There is only one report of central nervous system vasculitis associated with myelodysplastic syndrome,(10) that small vessel vasculitis confirmed by necropsy in brain, lung, and kidneys.

We describe a patient with MDS and vasculitis presenting with CNS medium vessel involvement. A clinical response to immunosuppressive therapy was also observed in the patient.

Case report

An 18- year- old patient with a history of anemia was admitted to our hospital because of headache, dysarthria, and severe paresis of right upper limb. 5 years ago, she was considered as MDS (refractory anemia type) by bone marrow aspiration (myeloid/erythroid= 1/3). Her problems began 2 months before admission with headache and diplopia on left ward gaze. Sagittal sinus thrombosis and parietal lobe infarction were identified by MRI. Anticoagulation therapy was started 6 weeks later. In July, she experienced another cerebral attack with severe headache, dysarthria, convulsion and right upper limb paresis. The patient readmitted by neurologist and anticonvulsant therapy was added to her management. In this time she was referred to rheumatologist for more workup.

On clinical examination, the patient presented with severe dysarthria, diplopia, irritability and depressed mood and affect. The force of right upper extremity was as 0/5 but lower extremities were normal in strength. Vital signs included; blood pressure: 100/60 mmHg, pulse rate: 80 beat/min, temperature 36.5˚C and respiratory rate 16 breaths per minute. The remaining physical findings included ear, nose, throat, cardiovascular and pulmonary systems were all normal except for pale skin.

Routine laboratory tests included:

Hemoglobin (Hg): 7.3, white blood cell count (WBC): 2000, platelets count (Plt): 134000 and

erythrocyte sedimentation rate (ESR): 71. Serum creatinine: 0.4 and 24- hour collection of urine contained 170 milligrams protein. A bone marrow aspiration showed dyserythropoesis as nucleocytoplasmic dissociation, nuclei budding and binucleation and she was considered as probably MDS (figure 1). The Myeloid/Erythroid ratio was 0.5 (normal range: 1.5-4.5). To initially rule out an infectious disease, blood, urine, and bone marrow cultures did not show any pathogen. Serological tests for brucellosis and typhoid fever were negative. No antibodies to human deficiency virus or hepatitis B or C were detected. Transesophageal echocardiography did not show any vegetation and chest X ray, ultrasound of abdomen as well as pelvis did not yield any abnormality. The patient who underwent an MRI showed evidence of thrombosis, hemorrhagic and ischemic damage with edema. Lumbar puncture was not done because of mass lesion identified by MRI. In this time the patient was treated with dexamethasone, phenytoin, ceftriaxon, clindamycine and enoxaparine.

The results of immunology tests were negative for RF, Anti CCP, ANA, anti ds DNA, C and P ANCA, anti sm, anti Ro/SSA, anti La/SSB, anticardiolipin antibodies and direct and indirect coombs' test. Three days after admission, neurological deficits were progressed acutely with right facial and lower limb hemiparesis. Then subsequently, the patient's condition deteriorated. MRI findings according to disease course are shown in figure 2.

The treatment was started on IV pulse therapy with methyl prednisolone (1000 mg/day) for 3 days and then the patient was given cyclophosphamide (1000 mg) on 4th day. Two days after the beginning of IV methyl prednisolone, paresis in lower limb and face was improved and wonderfully force of right upper limb changed to 2/5. In this time, CBC included: Hg: 9.5, WBC: 4600, plt count: 206000 and erythrocyte sedimentation rate: 21. The treatment continued by oral prednisolone (1mg/kg/day) and monthly IV cyclophosphamid. In second month of treatment, the patient could speak fluently and force of upper limb was as 4-4.5/5. We tapered steroid but below 15 mg patient's headache and anemia became more severe, so this dose of prednisolone was continued. After 12 months cyclophosphamide was changed to azathioprine and after 3 months lab data included: Hg: 8.5, WBC: 5900, plt count: 191000 and erythrocyte sedimentation rate: 23.

Discussion

Vasculitis is a heterogeneous group of clinical disorders in which an inflammation of the blood vessel develops that may cause necrosis, aneurismal dilatation, stenosis, thrombosis and hemorrhage.(10) In practice, primary systemic vasculitides are classified according to their clinical presentations, histological features and the size of affected vessels.

CNS vasculitis is characterized by inflammatory damage to blood vessel walls in the brain and spinal cord and is classified as a vasculitis of medium-sized vessels,(11) resulting in symptoms and signs of CNS dysfunction. Primary angitis of the CNS (PACNS) is defined as inflammation of the cerebral vasculature without angiitis in other organs. The disease is more common in females and in case series the average age is about 42 years.(12, 13) The initial presentations are headache, encephalopathy and stroke. Moreover, multiple strokes may be found in varying ages.(11) In 2/3 of cases ESR is elevated.(14)

There are some reports about association of vasculitis and MDS,(1, 2, 4, 6-10) but there is only one case report of PACNS-like vasculitis.(10) Theories about mechanisms of autoimmunity and vasculitis associated with MDS include:

Immune deregulation and synthesis of auto antibodies due to abnormalities in T and B cells, immune complex- mediated due to impairment of macrophage- mediated clearance, defective neutrophil function and production of cytokines by abnormal lymphocytes and monocytes as well as prior exposure to chemotherapy or radiotherapy.(10)

MRI which is the most sensitive but not specific imaging method for detecting PACNS, is abnormal in approximately 90% of cases. The lesions appear as mass lesions or areas of signal change. It is reasonable to recommend brain biopsy for those who have a slow onset, severe neurologic impairment, striking cerebrospinal fluid abnormalities or for patients who have failed to respond to corticosteroid therapy.(11) The fulminated progression of neurologic deficits did not allow us to take brain biopsy but disease progression despite anticoagulation therapy, cytopenia, elevated ESR and dramatic response to immunosuppression therapy, are strong reasons for such an autoimmune phenomenon.

Combination therapy with prednisolone and cyclophosphamide for at least one year is recommended(1, 12, and 14) and early initiation of treatment improves the prognosis.(14)

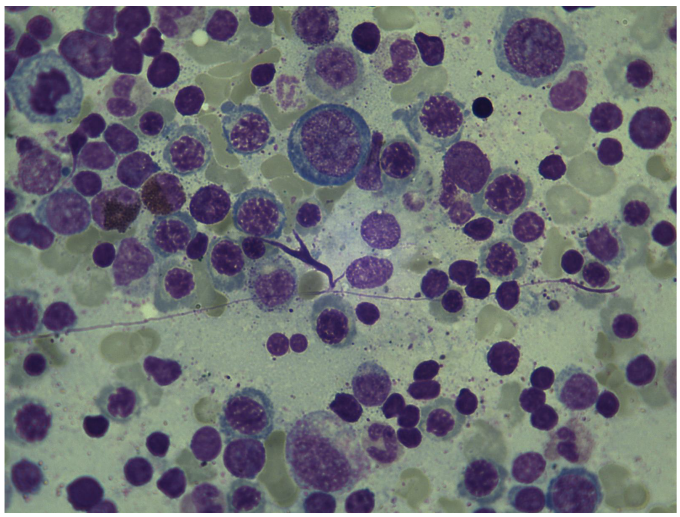

Figure- 1. Bone marrow aspiration showed dyserythropoesis as nucleocytoplasmic dissociation, nuclei budding and binucleation and she was considered as probably MDS.

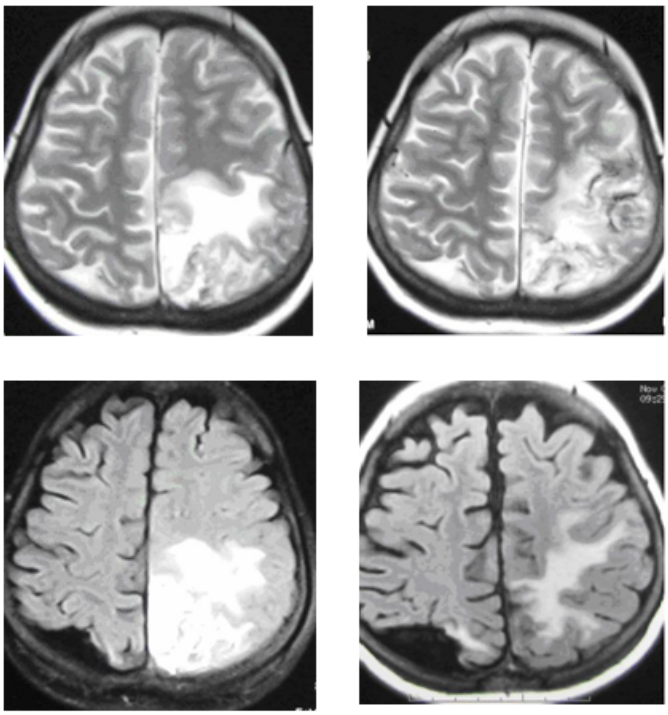

Figure- 2. MRI findings according to disease course are shown.

In this study we described a patient with MDS and PACNS-like vasculitis. According to our knowledge, it is the second report of CNS vasculitis in MDS in literature. We started prednisolone and cyclophosphamide early in the disease course. Due to young age, dramatic and persistent response to immunosuppression, the patient was different from other case reports.

Reference

1. Enright H, Jacob HS, Vercellotti G, et al. Paraneoplastic Autoimmune Phenomena in Patients with Myelodysplastic Syndrome: Response to Immunosuppressive Therapy. Br J Haematol, 1995; 91(2):403-8.

2. Castro M, Conn DL, Su WP, Garton JP. Rheumatic Manifestations in Myelodysplastic Syndromes. J Rheumatol. 1992; 19 (6): 1005-6.

3. Saitoh T, Murakami H, Uchiumi H, et al. Myelodysplastic Syndromes with Nephrotic Syndrome. Am J Hematol. 1999; 60(3):200-4.

4. Maeda Y, Arakawa K, Araki E, et al. Polymyositis and Cutaneous Vasculitis in a Patient with Myelodysplastic Syndrome. Rinsho Shinkeigaku. 1999; 39 (6): 639-42.

5.Onho E, Ohtsuke E, Watanabe K, et al. Behcet Disease Associated with Myelodysplastic Syndromes. A Case Report and a Review of the Literature. Cancer. 1997; 15; 79(2): 262-8.

6. DAS M, Chhabra R, Hinton SW. Cutaneous Leukocytoclastic Vasculitis and Myelodysplastic Syndrome with Little or no Evidence of Associated Autoimmune Disorders-a Case Report and a Brief Review of the Literature. Am J Med sci. 2008; 336 (4):368-71.

7. Fernandez-miranda C, Garcia- Marcilla A, Martin M, Gil R, et al. Vasculitis Associated with a Myelodysplastic Syndrome: A Report of 5 Cases. Med clin (Barc). 1994; 29; 103 (14):539-42.

8. Fain O, Hamidou M, Cacoub P, et al. Vasculitis Associated with Malignancy: Analysis of Sixty Patients.

9. Steurer M, Fritsche G, Tzankov A, et al. Large-Vessel Arteritis and Myelodysplastic Syndrome: Report of Two Cases. Eur J haematol. 2004; 73(2): 128-33.

10.Incalzi RA, Arena V, Capelli A, Gambassi G. Isolated PACNS-like Presentation of a Systemic Vasculitis Complicating a Myelodysplastic Syndrome. Journal of Internal Medicine. 2004; 255: 674-679.

11- Hellmann DB. Vasculitis of the Central Nervous System. In: Imboden J, Hellmann D, Stone J. Current Rheumatology Diagnosis and Treatment. 2nd ed. New York: Mc Graw Hill; 2007.321-325.

12.Kluck JJ, ter Berg JW, van der Laan RT, Krijne-Kubat B. Two Patients with Isolated Vasculitis of the Central Nervous System. Ned Tijdschr Geneeskd. 2002; 9; 146(10):482-6.

13. Kraemer M, Berlit P. Primary Central Nervous System Vasculitis: Clinical Experience with 21 New European Cases. Ann Rheum dis. 2000; 59(6):478-82.

14. Hallak H, Fressinaud C, Emile J. Isolated Angitis of the Central Nervous System. Report of Two Cases and Review of the Literature. Rev Neurol (Paris). 2002; 158 (11):1071-81.